REMARKS

I. Support for the Amendments

Claims 7, 16, and 35 have been amended. Claim 7 was amended in accordance with the Examiner's request, as discussed *infra*. Claims 16 and 35 have been amended to correct typographical or grammatical errors. Claim 16 previously had step d listed twice and an "and" omitted. Claim 35 previously had two omissions of the word "and".

Support for amended claims 7, 16, and 35 can be found in the original specification and claims. Additional support for amended claims 7, 16, and 35 can be found, e.g., on pages 5-9; on page 6, lines 3-12; on page 16, lines 1-7; from page 16, line 18, to page 20, line 20; and in the Examples. Additional support for amended claims 16 and 35 can be found, e.g., from page 10, line 31, to page 11, line 3; on page 11, lines 8-17; on page 12, lines 4-5; from page 12, line 33, to page 13, line 1; on page 15, lines 1-16; on page 16, lines 1-7; from page 16, line 18, to page 17, line 4; from page 17, line 32, to page 20, line 32; and in the Examples. Additional support for amended claim 16 can be found, e.g., on page 6, lines 3-12; on page 7, lines 11-26; on page 16, lines 1-16; and on page 22, lines 1-5. Additional support for amended claims 7 and 35 can be found, e.g., on pages 5-9; on page 6, lines 3-12; on page 16, lines 1-7; from page 16, line 18, to page 20, line 20; and in the Examples. Additional support for amended claim 35 can be found, e.g., on page 9, lines 18-28; from page 17, line 21, to page 18, line 4; and in the Examples.

II. Status of the Claims

Claims 1-34 were originally in the application, with claims 1, 5-8, 11, 16, 19, 21, 28, 33, and 34 being the independent claims. Claims 1-4 and 6-32 were elected with traverse in Response to the Election/Restriction Requirement, with claims 1, 7, 8, 11, 16, 19, 21, and 28 being the independent claims.

In the Office Action mailed 26 December 2002, the Examiner rejected claims 1-4 and 6-32, which were all the remaining claims. In the previous Amendment, filed Jun 20, 2003, claims 1, 6, and 28 were canceled, and non-elected claims 5, 33, and 34 were withdrawn without prejudice to the pursuit of such claims in a suitable continuing application.

Currently, claims 2-4, 7-27, 29-32, and 35-43 are pending in the application, with claims 7, 8, 11, 16, 19, 21, 30, and 35 being the independent claims.

Claims 2-4 and 9-10 are now dependent on claim 7. Claims 12-15 are dependent on claim 11. Claims 17 and 18 are dependent on claim 16. Claim 20 is dependent on claim 19. Claims 22-27 are dependent on claim 21. Claims 29 and 31-32 are dependent on claim 30. Claims 36-43 are dependent on claim 35 or on claims dependent on claim 35.

III. Rejection of Claims 2-4, 7, and 9-10 Under 35 U.S.C. § 112, Second Paragraph is Accommodated

The Examiner has rejected claims 2-4, 7, and 9-10 under 35 U.S.C. §112, second paragraph (pp. 2; par. 5 (and 5A1)). The Examiner alleges:

> Claims 2-4, 7, 9-10 are indefinite over the recitation "the solid medium" because it is unclear which of the two solid mediums set forth in the claims is being referred to in step d. (P. 2, par. 5 (A1).)

Claim 7 has been amended in response to the Examiner's rejection of these claims under 35 U.S.C. 112, second paragraph. (Claims 2-4 and 9-10 are dependent on claim 7.)

Applicants respectfully submit that the present claims 2-4, 7, and 9-10 fulfill the requirements of 35 U.S.C. §112, second paragraph, and request the Examiner's reconsideration of these claims accordingly.

IV. Rejection of Claims 2, 4, 7, 10, 35-36, 38-40, and 42-43 Under 35 U.S.C. § 102(e) is Traversed

The Examiner has rejected claims 2, 4, 7, 10, 35-36, 38-40, and 42-43 under 35 U.S.C. §102(e) as being anticipated by Robertson (U.S. Patent 6,153,104; November 28, 2000). Applicants respectfully disagree.

The Examiner alleges:

> Robertson teaches a method of body fluid separation. The methods uses a device comprising a chamber, a cooperating filter, a second chamber, where the first and second chamber has a connection to vacuum with filters on each side and a removable closure in the form of end caps. As seen in Figure 1 the device is provided. Robertson teaches that the invention provides equipment of notable simplicity and relatively low cost with method steps well within the capabilities of junior members of laboratory staff, to enable separation of a body fluid into various of its component (col. 1, lines 30-35). Robertson teaches obtaining a biological sample, namely a whole blood sample (limitations of 35a). The biological sample is in a suspension comprising genetic material, as whole blood is comprised of plasma, serum and cells (limitations of Claim 35b, 38). An apparatus comprising a chamber, two solid mediums, a vacuum means where the

second filter has a composition sorbed thereon. The matrix may comprise water, water/isotonic saline or cell detergent (col. 2, lines 40-50) (limitations of Claim 35c, 36). The whole blood sample is applied to one side of a filter, vacuum is applied to the opposite side of the filter to draw the whole blood sample there through and separate the plasma and red cell content of the blood from the leukocyte cell content, leaving the leukocyte content trapped in the filter (col. 2, lines 30-50) (limitations of Claim 35d, e). Following lysing, the chamber is inverted and the saline is applied to the opposite side of the filter to wash out the cell contents of the leukocyte cells from the filter into an appropriate receptacle from whether the DNA content is removed. Robertson teaches that to gather the cell contents of the leukocyte cells, it is most desirable that a filter membrane is provided to isolate the DNA content of the cells form other cell debris washed from the filter (col. 4, lines 60-65) (limitations of Claim 10, 42-43). Thus the genetic material is retained on the second solid medium. Robertson teaches that once the cells have been isolated, probes and further techniques may be used for analyzing the genetic material (col. 5) (limitations of Claim 40). (Pp. 3-4, par. 6.)

Applicants respectfully disagree with the Examiner's comments and traverse the anticipation rejection.[1]

It should be noted that the language of claim 7 presently reads as follows:

7 (currently amended). A method of genetic analysis, wherein the method comprises:

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[1] The Examiner has cited the present version of 35 U.S.C. §102(e), which states:

A person shall be entitled to a patent unless -

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351 (a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Applicants respectfully note that the present form of 35 U.S.C. §102(e) does not apply to patents resulting from an international application filed before 29 November 2000. Robertson (U.S. Patent 6,153,104; U.S.S.N. 08/836,942) was filed as PCT/GB95/02599 on 6 November 1995.

a. upstream processing of a biological sample to produce a suspension comprising cells comprising genetic material;

b. applying the suspension to a first solid medium;

c. contacting the cells on the first solid medium with a second solid medium comprising:

i. a matrix; and

ii. ***a composition sorbed to the matrix, the composition comprising preserving means for protecting genetic material from degradation;***

d. sorbing the genetic material to the second solid medium; and

e. analyzing the genetic material. (Emphasis added.)

Similar language is used in claim 35 with respect to the "composition sorbed to the matrix:"

35 (currently amended). A method of detecting and analyzing genetic material from a biological sample, wherein the method comprises:

a. obtaining a biological sample;

b. processing the biological sample to produce a suspension of one or more cells or virions comprising genetic material;

c. providing an apparatus comprising:

i. a chamber for containing a fluid including a suspension of cells or virions therein, the chamber comprising:

- an opening therethrough; and
- a first solid medium removably disposed over the opening;

ii. vacuum means for drawing the fluid from the chamber and through the first solid medium and depositing the cells or virions on the first solid medium;

iii. a second solid medium comprising:

- a matrix; and
- ***a composition sorbed to the matrix, the composition comprising preserving means for protecting the genetic material from degradation***;

d. placing a fluid comprising the suspension in the chamber;

e. using the vacuum means to draw the fluid from the chamber and through the first solid medium and to deposit the cells or virions on the first solid medium;

f. contacting the cells or virions on the first solid medium with the second solid medium;

g. releasing the genetic material from the cells or virions and retaining the genetic material with the second solid medium; and

h. analyzing the genetic material. (Emphasis added.)

Applicants respectfully submit that a rejection under §102(e) requires the reference to contain each and every element of the rejected claim. While Robertson (see, e.g., cols. 4-5) describes the use of "water, isotonic saline, an appropriate chemical lysing agent or a compatible cell detergent" to lyse **leukocytes <u>after</u> they have been already entrapped** within the filter, **it does <u>not</u> describe a "composition sorbed to the matrix"** to which a **sample is subsequently exposed.** In at least **one embodiment**, Robertson **does not lyse the cells at all** (col. 2, ll. 63-65). Moreover, the method of **Robertson requires the use of at least two chambers** separated by a filter (claims).

Furthermore, with respect to claim 4, Robertson does not specifically mention dissociation of cells during upstream processing of the sample.

Finally, the Examiner's argument that the invention of Robertson "provides equipment of notable simplicity and relatively low cost with method steps will within the capabilities of junior members of laboratory staff" is irrelevant to the requirements of 35 U.S.C. §102.

Applicants respectfully submit that the present claims 2, 4, 7, 10, 35-36, 38-40, and 42-43 fulfill the requirements of 35 U.S.C. 102(e) and request the Examiner's reconsideration of these claims accordingly.

V. Rejection of Claims 2, 7, and 10 Under 35 U.S.C. § 102(b) is Traversed

The Examiner has rejected claims 2, 7, and 10 under 35 U.S.C. §102(b) as being anticipated by Alberts (Molecular Biology of the Cell, 3rd edition, 1994). Applicants respectfully disagree.

The Examiner alleges:

> Alberts teaches a method of analyzing cells by DNA cloning. DNA fragments are inserted into the purified DNA genome of a self-replicating genetic element-generally a virus or a plasmid, upstream processing of a biological sample (page 308). The bacteria is plated out on medium containing antibiotic and let to grow (page 309). **Culturing dishes containing growing bacterial colonies are blotted with a piece of filter paper (second solid medium). The paper is treated with alkali to disrupt the cells** and incubated with labeled DNA probe. As seen in Figure 7-26, two solid mediums are used which allow for genetic analysis. Thus, since Alberts teaches every limitation of the claims, Alberts anticipates the claimed invention. (Pp. 4-5, par. 7; emphasis added.)

Applicants respectfully disagree with the Examiner's comments and traverse the anticipation rejection.

The Examiner has rejected claims 2, 7, and 10 under 35 U.S.C. §102(b) in view of Alberts, but a rejection under §102(b) requires the reference to contain each and every element of the rejected claim. Again, claim 7, upon which claims 2 and 10 are dependent, presently reads as follows:

> 7 (currently amended). A method of genetic analysis, wherein the method comprises:
>
> a. upstream processing of a biological sample to produce a suspension comprising cells comprising genetic material;
>
> b. applying the suspension to a first solid medium;
>
> c. contacting the cells on the first solid medium with a second solid medium comprising:
>
> i. a matrix; and
>
> *ii.* ***a composition sorbed to the matrix, the composition comprising preserving means for protecting genetic material from degradation;***
>
> d. sorbing the genetic material to the second solid medium; and
>
> e. analyzing the genetic material. (Emphasis added.)

The excerpt from Alberts, which was cited by the Examiner, makes no mention of a second medium comprising a matrix and "a composition sorbed to the matrix, the composition comprising preserving means for protecting genetic material from degradation." Rather, it describes "filter paper" (p. 312) or "absorbent paper" (Fig. 7-26, p. 313), which is used for blotting a culture dish and to which "some members of each bacterial colony adhere" (p. 312). **After** the cells adhere, "[t]he adhering colonies, known as *replicas*, are treated with alkali to disrupt the cells and to separate the strands of their DNA molecules..." (p. 312, emphasis in original; see also Fig. 7-26, p. 313). Nowhere is there a description of "a composition sorbed to the matrix" and "comprising preserving means for

protecting genetic material from degradation." Instead, in Alberts, the replica is made and **only afterwards** is it treated with alkali.

Applicants respectfully submit that the present claims 2, 7, and 10 fulfill the requirements of 35 U.S.C. 102(b) and request the Examiner's reconsideration of these claims accordingly.

VI. Rejection of Claims 3, 8-9, 16, 19, 21, 29-32, 37, and 41 Under 35 U.S.C. § 103(a) Is Traversed

The Examiner has rejected claims 3, 8-9, 16, 19, 21, 29-32, 37, and 41 under 35 U.S.C. 103(a) as being unpatentable over Robertson (U.S. Pat. 6,153,105 (Nov. 28, 2000)) in view of Burgoyne (U.S. Pat. 5,807, 527 (Sept. 1998)). Applicants respectfully disagree.

The Examiner alleges:

> Robertson teaches a method of body fluid separation. The methods uses a device comprising a chamber, a cooperating filter, a second chamber, where the first and second chamber has a connection to vacuum with filters on each side and a removable closure in the form of end caps. As seen in Figure 1 the device is provided. Robertson teaches that the invention provides equipment of notable simplicity and relatively low cost with method steps well within the capabilities of junior members of laboratory staff, to enable separation of a body fluid into various of its component (col. 1, lines 30-35). Robertson teaches obtaining a biological sample, namely a whole blood sample (limitations of 35a). The biological sample is in a suspension comprising genetic material, as whole blood is comprised of plasma, serum and cells (limitations of Claim 35b, 38). An apparatus comprising a chamber, two solid mediums, a vacuum means where the second filter has a composition sorbed thereon. The matrix may comprise water, water/isotonic saline or cell detergent (col. 2, lines 40-50)(limitations of Claim 35c, 36). The whole blood sample is applied to one side of a filter, vacuum is applied to the opposite side of the filter to draw the whole blood sample there through and separate the plasma and red cell content of the blood from the leukocyte cell content, leaving the leukocyte content trapped in the filter (col. 2, lines 30-50)(1 imitations of Claim 35d, e).

Following lysing, the chamber is inverted and the saline is applied to the opposite side of the filter to wash out the cell contents of the leukocyte cells from the filter into an appropriate receptacle from whether the DNA content is removed. Robertson teaches that to gather the cell contents of the leukocyte cells, it is most desirable that a filter membrane is provided to isolate the DNA content of the cells form other cell debris washed from the filter (col. 4, lines 60-65)(limitations of Claim 10, 42-43). Thus the genetic material is retained on the second solid medium. Robertson teaches that once the cells have been isolated, probes and further techniques may be used for analyzing the genetic material (col. 5)(limitations of Claim 40).

Robertson does not specifically teach using the preserving means which contains a weak base, a chelating agent or an anionic surfactant or detergent. (Pp. 6-7, par. 9; emphasis added.)

The Examiner then relies upon Burgoyne '527 to supply the deficiencies of Robertson as follows:

However, Burgoyne teaches a method of storage of DNA using solid medium having a compound which protects against degradation of DNA incorporated into or absorbed on the matrix, and for recovery of DNA or in situ use of DNA (abstract). Blood dried onto filter paper is a proven alternative and has been shown that DNA can be extracted and isolated from dried blood spots in a form and in sufficient quantities for use in DNA analysis (col. 1, lines 60-65). Burgoyne teaches that the solid matrix may comprise a solid support such as an absorbent cellulose-based paper or a micromesh of synthetic plastics material. Moreover, Burgoyne teaches that the solid medium comprises a composition comprising a weak base, a chelating agent and an anionic surfactant or detergent (col. 2, lines 60-64)(limitations of Claim 3). DNA on filter paper specially treated in accordance with this invention was purified in situ, then subjected to the polymerase chain reaction (col. 4, lines 37-30). Burgoyne teaches that treated paper was much more efficient than untreated paper. Treated paper gave recoveries of approximately 100% where as untreated paper only has about 10% recovery (col. 6, lines 8-10). Burgoyne teaches that exon 2 of the nRAs protoconcogene and male specific Y chromosome repeat, were genotyped (limitation of Claim 2). Burgoyne teaches that DNA may be stored on the solid matrix having a composition thereon are suited for performance under automated conditions. **Burgoyne teaches that the means of storage may be established for long term storage and may be kept in orderly, low-volume files** (col. 4-5). (Pp. 7-8, par. 9; emphasis added.)

The Examiner alleges further:

> There, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Robertson to use the composition taught by Burgoyne for lysing cells. **Burgoyne teaches the benefits of using the solid support for storage of DNA for long periods of time. The benefits of the storage of the DNA upon the solid matrix additional includes the low-volume files as compared to liquid blood samples which require more care.** Therefore, the ordinary artisan would have been motivated to have purified leukocytes from blood using the particular composition taught by Burgoyne for the expected benefit of diagnostic importance. (P. 8; par. 9; emphasis added.)

Applicants respectfully disagree with the Examiner's comments and traverse the obviousness rejection.

Robertson has been discussed at length, *supra*, with respect to the Examiner's rejection under 35 U.S.C. §102(e), and the arguments outlined in that discussion likewise apply here, particularly with respect to the absence of a "composition sorbed to the matrix." Here, the Examiner is attempting to use Burgoyne to supply the deficiencies of Robertson. On the contrary, however, Robertson never even addresses the issue of "storage" of DNA ("long-term" or otherwise), let alone the desirability of maintaining DNA "in orderly, low-volume files." In fact, as the Examiner notes, the teaching of Robertson regarding "liquid blood samples which require more care," not to mention liquids in general, such as the need to apply "water, isotonic saline, an appropriate chemical lysing agent or a compatible cell detergent" to the filter in order to achieve lysis of the cells and subsequent release of the DNA, teaches away from the present invention. Moreover, the method and apparatus of Robertson require the use of at least two chambers to hold the liquids used, whereas in the present invention, a piece of the second solid medium comprising the preserving means may, in one embodiment, simply be used as a wipe or a swab to collect DNA from cells isolated on the first solid medium.

Likewise, there is **no suggestion in either** of the references **to combine the teachings of Robertson with Burgoyne**. As noted *supra*, Robertson simply discloses a method of isolating cells using a filter and then optionally lysing them using liquid chemical treatments. There is no suggestion of a solid medium comprising a matrix with a **composition already sorbed to the matrix prior to contact with cells** in a sample. In contrast, **Burgoyne focuses on the application of whole cells onto a treated solid medium capable of lysing the cells directly without the need for a liquid lysate**. As a result, **Burgoyne teaches away from Robertson**, because one of ordinary skill in the art reading Robertson would assume that, because the method of Robertson requires isolation of the cells on the filter prior to lysis with a liquid chemical treatment, it would not be applicable for the treated solid medium of Burgoyne, resulting in **a doubling of the lysis steps**.

Moreover, the Examiner notes that the medium of Burgoyne is suitable for "for performance under automated" and can provide "long-term, low-volume storage, automation and ease in handling specimens," but the present invention with two solid media is more complex in structure and usage.

Applicants respectfully submit that the present claims 3, 8-9, 16, 19, 21, 29-32, 37, and 41 fulfill the requirements of 35 U.S.C. §103(a) and request the Examiner's reconsideration of these claims accordingly.

VII. Clarification of Non-Allowance of Claims 11-15, 17-18, 20, and 22-27 Is Requested

The Examiner has concluded that no claims are allowable over the art (p. 8; par. 10). As discussed *supra*, the Examiner has rejected claims 2-4, 7, and 9-10 under 35 U.S.C. §112, second paragraph; claims 2, 4, 7, 10, 35-36, 38-40, and 42-43 under 35 U.S.C. §102(e); claims 2, 7, and 10 under 35 U.S.C. §102(b); and 3, 8-9, 16, 19, 21, 29-32, 37, and 41 under 35 U.S.C. §103(a).

Claims 11-15, 17-18, 20, and 22-27 are not specifically rejected. Claim 11 is an independent claim, and claims 12-15 are dependent on claim 11. Claims 17 and 18 are dependent on rejected claim 16; claim 20 is dependent on rejected claim 19; and claims 22-27 are dependent on rejected claim 21. Applicants respectfully note that the Examiner has not rejected or indicated any grounds of rejection for claims 11-15, 17-18, 20, and 22-27, although the Examiner has stated that no claims are allowable over the art. As a result, Applicants are unable to respond to any rejection of these claims.

VIII. Conclusion

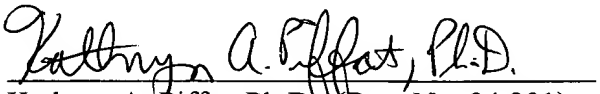
It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants believe that no extension of time is required. If, however, a petition for an additional extension of time is required, then the Examiner is requested to treat this as a conditional petition for an additional extension of time. Although it is not believed that any fee is required, in addition to the fee submitted herewith, to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

Date: January 15, 2004



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